

# ***HUMAN SUBJECTS RESEARCH “SECTION E”***

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# *Human Subjects in Research-Outline*

## Prior to Submission

- Office for Human Research Protections (OHRP)
- Requirements when involving human subjects in research
- How to determine if your research involves Human Subjects

## For the Application/Proposal

- Human Subjects in Research Studies/Clinical Trials
- How to write Human Subject sections
- Inclusion of Women, Minorities and Children in Research

## Primary website sources:

- OHRP: <http://www.hhs.gov/ohrp>
- NIAID Human Subjects in Research Standard Operating Procedure (SOP): <http://www.niaid.nih.gov/ncn/sop/hs.htm>
- NIAID: How to Write a Human Subjects Application:  
<http://www.niaid.nih.gov/ncn/clinical/humansubjects/default.htm>



# Grant Application Face Page

Department of Health and Human Services Public Health Services <b>Grant Application</b> <i>Do not exceed character length restrictions indicated.</i>		<b>LEAVE BLANK—FOR PHS USE ONLY.</b>		
		Type	Activity	Number
		Review Group		Formerly
		Council/Board (Month, Year)		Date Received
1. TITLE OF PROJECT (Do not exceed 81 characters, including spaces and punctuation.)				
2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION <input type="checkbox"/> NO <input type="checkbox"/> YES (If "Yes," state number and title)				
Number: Title:				
3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR			New Investigator <input type="checkbox"/> No <input type="checkbox"/> Yes	
3a. NAME (Last, first, middle)			3b. DEGREE(S)	3h. eRA Commons User Name
3c. POSITION TITLE			3d. MAILING ADDRESS (Street, city, state, zip code)	
3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT				
3f. MAJOR SUBDIVISION				
3g. TELEPHONE AND FAX (Area code, number and extension)			E-MAIL ADDRESS:	
TEL: FAX:				
4. HUMAN SUBJECTS RESEARCH		4b. Human Subjects Assurance No. Put your FWA number here		
<input type="checkbox"/> No <input checked="" type="checkbox"/> Yes		4c. Clinical Trial <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes		
4a. Research Exempt		4d. NIH-defined Phase III Clinical Trial <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes		
<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes		If "Yes," Exemption No. NA		
5. VERTEBRATE ANIMALS <input type="checkbox"/> No <input type="checkbox"/> Yes				
5a. If "Yes," IACUC approval Date		5b. Animal welfare assurance no.		
NA		NA		
6. DATES OF PROPOSED PERIOD OF SUPPORT (month, day, year—MM/DD/YY)		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT
From	Through	7a. Direct Costs (\$)	7b. Total Costs (\$)	8a. Direct Costs (\$)
				8b. Total Costs (\$)
9. APPLICANT ORGANIZATION		10. TYPE OF ORGANIZATION		



# *Office for Human Research Protection (OHRP)- Mission (<http://www.hhs.gov/ohrp>)*

The Office for Human Research Protections (OHRP) provides leadership and oversight on all matters related to the protection of human subjects participating in research conducted or supported by the U.S. Department of Health and Human Services (HHS) to ensure such research is conducted with the highest ethical standards.

- International Issues (<http://www.hhs.gov/ohrp/international>)
- OHRP provides quality improvement consultation and research ethics training to domestic and foreign institutions involved in international biomedical and behavioral research to help ensure that recognized ethical protections are afforded to persons participating in research conducted in countries outside the United States.



# *Human Subject Certifications and Assurances*

For projects involving human subjects research, applicants and offerors must obtain the following certifications and assurances to comply with NIH requirements:

- Federalwide Assurance (FWA).
- Assurance of Office of Research Integrity (ORI) Compliance.
- Certification of Institution Review Board (IRB) for domestic applications or Independent Ethics Committee (IEC) for foreign applications.
- Certification of Investigator Training in Protection of Human Subjects.



# ***Federalwide Assurance (FWA)***

*(<http://www.hhs.gov/ohrp>, then click "Assurances" or  
[http://www.hhs.gov/ohrp/assurances/assurances\\_index.html](http://www.hhs.gov/ohrp/assurances/assurances_index.html))*

- This is a two-step process.
  - First, your institution must ensure that the IRB(s)/IECs you designate under the FWA are registered with OHRP. If not, they should submit the registrations. This can be done on the same electronic FWA application mentioned below.
  - Second, you must complete the FWA application.
- The electronic submission of an FWA application (<http://ohrp.cit.nih.gov/efile>) guides you through the two-step process.
- Read the Frequently Asked Questions (FAQs)- they have important information.
- For questions about using OHRP's electronic submission system, contact your regional or country coordinator:  
<http://www.hhs.gov/ohrp/daq-staff.html#staff>



# *Assurance of Office of Research Integrity (ORI) Compliance*

*(<http://ori.hhs.gov>)*

- Office of Research Integrity (ORI;) promotes integrity in biomedical and behavioral research supported by the U.S. Public Health Service. An institution must have an ORI assurance on file.
- Form: *<http://www.hhs.gov/forms/PHS-6349.pdf>*



# *Certification of IRBs / IECs*

- As mentioned, your institution must ensure that the IRB(s)/IEC(s) you designate under the FWA are registered with OHRP. If not, they should submit the registrations via the FWA application (<http://ohrp.cit.nih.gov/efile>).
- Then your Protection of Human Subject's plan needs to be approved. Although this is "just in time", the advice is to start early with this. Two helpful websites:
  - NIAID Human Subjects Certifications: IRB or IEC SOP <http://www.niaid.nih.gov/ncn/sop/irb.htm>
  - IRB and IEC Requirements for Foreign Countries <http://www.niaid.nih.gov/ncn/clinical/humansubjects/hs07.htm>

# *Certification of Training in the Protection of Human Subjects*

- If your human subjects application falls within the fundable range, you will need to obtain training in the protection of human subjects for your PI and key personnel.
- NIAID will request documentation of the training in the protection of human subjects just-in-time, after the application or proposal is approved for funding and before NIH issues an award. See the Just-in-Time SOP (<http://www.niaid.nih.gov/ncn/sop/jit.htm>)
- Document Training in Research Conduct: <http://www.niaid.nih.gov/ncn/clinical/humansubjects/hs20.htm>
- Human Subject's Certifications: Training SOP: <http://www.niaid.nih.gov/ncn/sop/hstraining.htm>



# *NIAID Human Subjects in Research SOP*

*<http://www.niaid.nih.gov/ncn/sop/hs.htm#cert> and  
[http://www.niaid.nih.gov/ncn/clinical/default\\_human.htm](http://www.niaid.nih.gov/ncn/clinical/default_human.htm)*

- Applicants and offerors must comply with all human subjects requirements.
- Grant applicants must follow human subjects instructions in the PHS 398 or the RFA or funding opportunity announcement (FOA).
- Contract offerors follow those in the RFP.
- Both applicants and offerors must also follow the instructions in the “NIAID Clinical Terms of Award” and for research in China, the “NIAID Clinical Terms of Award Restrictions for China” (see websites above).



# *Does your application/proposal involve Human Subjects?*

*<http://www.niaid.nih.gov/ncn/sop/hs.htm#cert>*

To help determine how this applies to your research, look at

- The HHS Human Subject Regulations Decision Charts:  
*(<http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm>)*
- The Decision Tree for Research Involving Private Information of Biological Specimens:  
*<http://grants.nih.gov/grants/policy/hs/PrivateInfoOrBioSpecimensDecisionChart.pdf>*

To view the decision trees reviewers use to see whether you have complied with requirements, see

- NIAID's other Decision Trees for Human Subjects Requirements:  
*<http://www.niaid.nih.gov/ncn/clinical/decisiontrees/default.htm>*
- Human Subjects Resources:  
*[http://www.niaid.nih.gov/ncn/clinical/default\\_human.htm](http://www.niaid.nih.gov/ncn/clinical/default_human.htm)*



# *Application/Proposal Preparation*

- In the Human Subjects Research section of the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets the requirements of the HHS regulations to protect human subjects from research risks and the requirements of NIH policies on inclusion of women, minorities, and children.

# *Application/Proposal Preparation*

- For all research involving human subjects, a part of the peer review process will include careful consideration of protections from research risks, as well as the appropriate inclusion of women, minorities, and children, based on the information in the application.

# Writing a Human Subjects Application

<http://www.niaid.nih.gov/ncn/clinical/humansubjects/default.htm>

- This NIAID web site has a step-by- step tutorial on writing the human subjects sections. Since NIH has not fully transitioned to the electronic submission, during the transition period, this tutorial refers to the hardcopy PHS 398.

Instructions you must follow for the paper PHS 398 form:

- Part II Supplemental Instruction for Preparing the Human subjects Section of the Research Plan:

<http://grants.nih.gov/grants/funding/phs398/HumanSubjects.doc>

- PHS 398: <http://grants.nih.gov/grants/funding/phs398/phs398.html>

- NOTE: While NIH moves to electronic applications, use either the PHS 398 or the Funding Opportunity Announcement (FOA depending whether the grant type you are applying for has transitioned to electronic submission. See the dates in NIH's Transition Plan on the Electronic Submission (<http://era.nih.gov/ElectronicReceipt/>) page.



# *Human Subjects Research*

## **PHS 398 Section E. Human Subjects Research**

- Protection of Human Subjects
- Data and Safety Monitoring Plan (for Phase III clinical trials or other trials and research with increased risk to the patient)
- Inclusion of Women and Minorities
  - Include Targeted/Planned Enrollment Table
- Inclusion of Children



# *Human Subjects Research*

- DATA SAFETY AND MONITORING PLAN

- REQUIREMENTS FOR NIH PHASE III TRIALS

(Note: For Phase III trials, the Women, Minority, and Children sections must each address whether differences between these groups of people are expected and able to be detected with the study as planned)



# *Human Subjects Research*

## ***PROTECTION OF HUMAN SUBJECTS***

*(not part of page limits of Research Plan)*

- RISKS TO THE SUBJECTS
  - Describe human subjects involvement and characteristics
  - Identify criteria for inclusion or exclusion of any subpopulation
  - Describe sources of human subject materials (specimens, records)
  - Describe and assess the likelihood and seriousness of potential risks to subjects
- ADEQUACY OF PROTECTION AGAINST RISKS
  - Describe plans for the recruitment of subjects and the process for obtaining informed consent
  - Describe planned procedures for protecting against or minimizing potential risks
- DISCUSS POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS
- THE IMPORTANCE OF THE KNOWLEDGE TO BE GAINED



# *Human Subjects Research*

## ***INCLUSION OF WOMEN AND MINORITIES***

- Participants in trials must be representative of populations most impacted by the disease within their geographic region
- Particular consideration given to gender and minority groups
- Include Targeted/Planned Enrollment Table

(See RFA language and PHS 398 Supplemental Instructions for Human Subjects pages 15-19

<http://grants.nih.gov/grants/funding/phs398/HumanSubjects.doc> )



# Human Subjects Research

## Inclusion Enrollment Report

**This report format should NOT be used for data collection from study participants.**

Study Title: \_\_\_\_\_  
 Total Enrollment: \_\_\_\_\_ Protocol Number: \_\_\_\_\_  
 Grant Number: \_\_\_\_\_

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race				
Ethnic Category	Sex/Gender			Total
	Females	Males	Unknown or Not Reported	
Hispanic or Latino				**
Not Hispanic or Latino				
Unknown (individuals not reporting ethnicity)				
<b>Ethnic Category: Total of All Subjects*</b>				*
<b>Racial Categories</b>				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				



# *Human Subjects Research*

**Children must be considered for inclusion in all human subject research supported by NIH**

Effective for all new applications received after  
October 1, 1998

- Child is defined as an individual under age 21
- If children are included, Investigator must address
  - ◆ age range
  - ◆ expertise of investigative team
  - ◆ facilities
  - ◆ sufficient numbers



# *Human Subjects Research*

**If children are not included, must justify exclusion**

- Policy  
<http://grants.nih.gov/grants/funding/children/children.htm>
- PHS 398 Supplemental Instructions for Human Subjects

